Microlog Microfiche Collection
Resolution Chart

Copyright

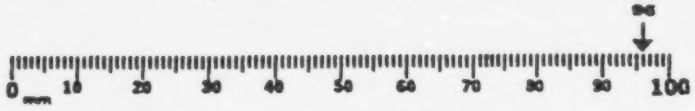
Copyright for the ***contents*** of this microfiche is held by the publisher of the original document. Please contact the original publisher for guidance in all copyright matters. Copyright in this ***microfiche edition*** is held by Micromedia Limited.

Quality of the Microfiche Reproduction

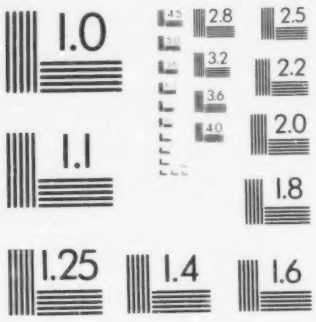
Micromedia Limited maintains the highest standards for micrographic reproduction. Attempts are made to obtain the best quality print version to microfilm. However, there are some printing styles, colours and graphic layout styles (including maps, graphs and tables) which do not reproduce well. Because of the value of the original document, Micromedia has filmed it recognizing that it may not be as easy to read as the original document.

Some pages have been filmed twice to improve the clarity of the reproduction. Consult both reproductions to ensure that all of the original text is read.

Microcopy Resolution Test Chart
National Bureau of Standards
Standard Reference Material 1010a
(ANSI and ISO Test Chart No. 2)



PM-1 3½"x4" PHOTOGRAPHIC MICROCOPY TARGET
NBS 1010a ANSI/ISO #2 EQUIVALENT



MS109

NATIONAL MICROGRAPHICS ASSOCIATION

24x

micromedia
a division of IHS Canada

20 Victoria Street, Toronto, ON M5C 2N8
Tel.: (416) 362-5211
Toll free: 1-800-387-2689
Fax: (416) 362-6161

Collection MICROLOG sur Micromédia
Tableau de résolution

Droits d'auteurs

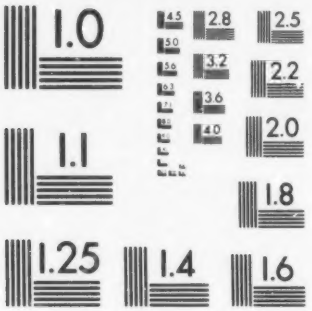
Les droits d'auteurs du conenu de cette microfiche sont détenus par l'éditeur du document original. Veuillez communiquer avec celui-ci pour obtenir des renseignements sur tout ce qui touche les droits d'auteurs. Les droits d'auteurs de cette édition sur microfiche sont détenus par Micromédia Limitée.

Qualité de reproduction sur microfiche

Micromédia Limitée maintient les normes de reproduction micrographique les plus élevées. Elle fait tout son possible pour obtenir la version sur papier à reproduire sur microfiche de la meilleure qualité possible. Cependant, certains styles d'imprimerie, de couleurs et de style de mise en page graphique (incluant des cartes, des grahiques et des tableaux) se reproduisent mal. En raison de la valeur du document original, Micromédia l'a reproduit tout en reconnaissant qu'il ne sera peut-être pas aussi lisable que le document original.

Tableau de résolution micrographique
National Bureau of Standards
Standard Reference Material 1010a
(ANSI and ISO Test Chart No. 2)

PM-1 3½"x4" PHOTOGRAPHIC MICROCOPY TARGET
NBS 1010a ANSI/ISO #2 EQUIVALENT



MS109

24x

NATIONAL MICROGRAPHICS ASSOCIATION

micromedia
a division of IHS Canada

20 Victoria Street, Toronto, ON M5C 2N8
Tel.: (416) 362-5211
Toll free: 1-800-387-2689
Fax: (416) 362-6161

© THE QUEEN'S PRINTER FOR ONTARIO
2000

REPRODUCED WITH PERMISSION

L'IMPRIMEUR DE LA REINE POUR L'ONTARIO

REPRODUIT AVEC PERMISSION

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

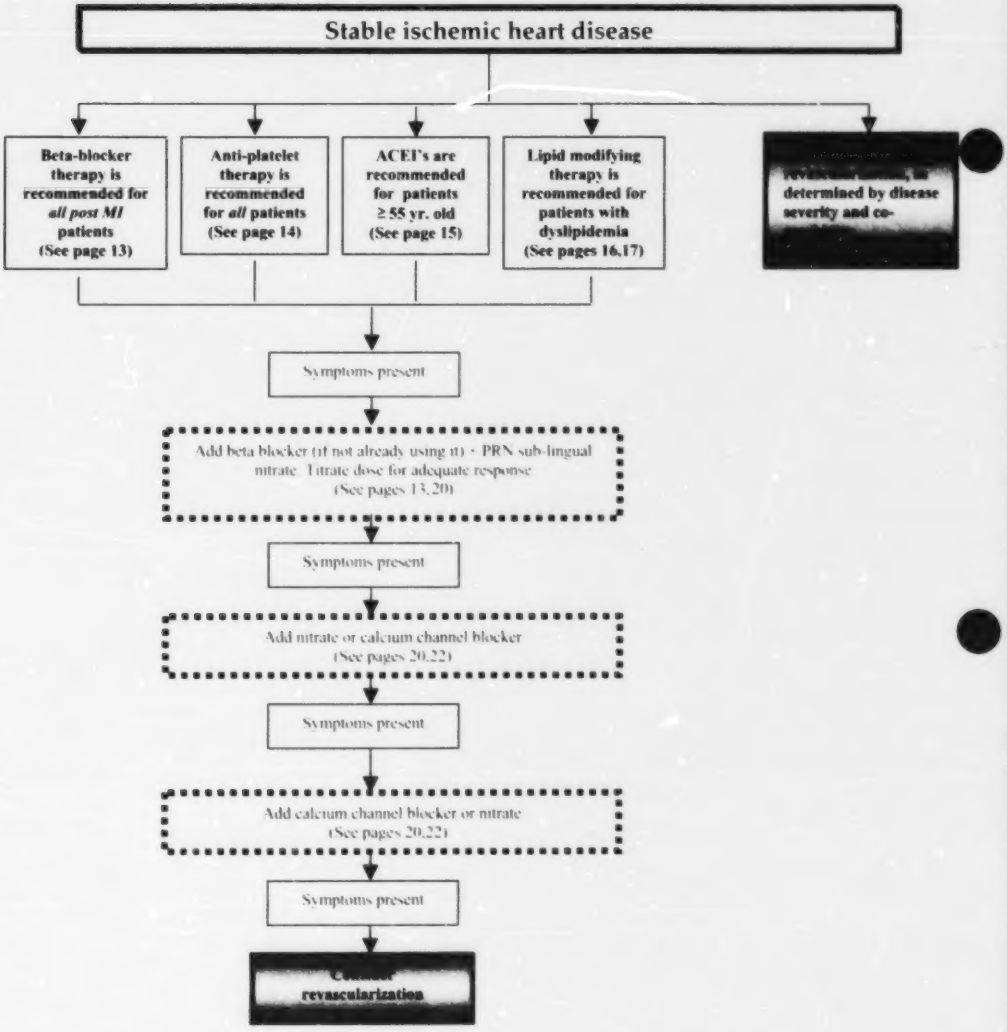
Published Fall 2000

1ST Edition

Ontario Drug Therapy Guidelines for Stable Ischemic Heart Disease in Primary Care

Ontario Program for Optimal Therapeutics

Guide to the Guideline


Stable ischemic heart disease
Beta-blocker therapy is recommended for *all post MI* patients (See page 13)
Anti-platelet therapy is recommended for *all* patients (See page 14)
ACEI's are recommended for patients ≥ 55 yr. old (See page 15)
Lipid modifying therapy is recommended for patients with dyslipidemia (See pages 16,17)
determined by disease severity and co-
Symptoms present
Add beta blocker (if not already using it) + PRN sub-lingual nitrate. Titrate dose for adequate response (See pages 13,20)
Symptoms present
Add nitrate or calcium channel blocker (See pages 20,22)
Symptoms present
Add calcium channel blocker or nitrate (See pages 20,22)
Symptoms present
revascularization
Disease modifying drug therapy procedure
Symptom modifying drug therapy
Disease or symptom modifying

Coexistence of modifiable risk factors such as *diabetes, hypertension, dyslipidemia* or *smoking* can lead to a multiplicative effect in occurrence of adverse cardiac outcomes. Risk factor modification can lead to a significant reduction in cardiac events.

107870

101-02442/

Ontario Drug Therapy Guidelines for Stable Ischemic Heart Disease in Primary Care

Ontario Program for Optimal Therapeutics

June, 2000

For additional copies please write or call:

PUBLICATIONS ONTARIO
50 Grosvenor St.
Toronto, Ontario M7A 1N8
Telephone: (416)-326-5300 or toll-free in Ontario 1-800-668-9938.
Hearing impaired call: (416)-965-5130 or toll-free in Ontario 1-800-268-7095
Fax: (416)-326-5317

MasterCard and Visa accepted. Cheques and money orders payable to the Minister of Finance. Prepayments required.

ISBN 1-894706-02-1

Acknowledgment: Support for the development, production and distribution of this guideline was provided by the Ontario Program for Optimal Therapeutics (OPOT), made possible through a grant from the Ontario Ministry of Health and Long-Term Care.

DISCLAIMERS -- PLEASE READ CAREFULLY: This publication is designed for use by qualified health practitioners in providing health services, and is made available upon the express understanding that the authors, publisher, and other parties involved in its preparation are not providing medical or other professional advice to the general public. If required, such advice should be sought from a qualified health practitioner. This publication is not intended to replace other prescribing information, or as a substitute for the knowledge of a qualified health care provider. Nor can the guidelines take into account the unique needs of each patient or the variations in clinical resources available to a particular community or health care professional. Physicians are urged to consult drug information available in the medical literature, and from the manufacturer and other sources before prescribing.

This publication is based on information from sources believed to be reliable. While great effort has been taken to assure the completeness and accuracy of the information, it is not intended to reprint all of the information available on the subject of the publication, but rather to compile, complement and supplement other available sources. The Review Panel, publisher, printer and others contributing to the preparation of this document cannot accept liability for errors, omissions or any consequences arising from the use of the information.

Inclusion of a pharmaceutical product in these guidelines was determined solely on the basis of the Review Panel's expert professional assessment of the available evidence. It is not intended, and cannot be taken, as a recommendation that the product be included in the reimbursement policies of any drug plan or benefits manager.

Stakeholder groups were invited to participate in the development of these guidelines by reviewing and commenting upon the guidelines in draft form. These included health care professionals, professional societies, the pharmaceutical industry and the Ontario Ministry of Health and Long-Term Care.

Comments: A form is provided at the end of the document for the submission of reader's suggestions.

© 2000 Queen's Printer of Ontario

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording, or otherwise, without the prior written permission of the publisher.

Table of Contents

Preamble 3

Introduction to stable ischemic heart disease 7
Risk factor modification and management
Criteria for 'disease modifying' vs. 'symptom modifying' therapy.
Algorithm-- A stepwise approach to drug management of
stable ischemic heart disease.

Disease modifying therapy 13
Therapeutic recommendations for disease modification including dose and average cost per day.

Symptom modifying therapy 20
Therapeutic recommendations for symptom modification including dose and average cost per day.

References 25

Appendices 29
List of commonly used brand names for different generic drug classes.
Synopsis of investigational and unproven therapies.
Nomogram for calculation of the Body Mass Index (BMI).

Comment Form 35

Preamble

Ontario Program for Optimal Therapeutics

Consensus Panel

The participants who have contributed towards the development of these 'Guidelines' are (in alphabetical order):

J. Malcolm Arnold, London, *ON*
Stephen Beamish, Elora, *ON*
Gregory Curnew, Hamilton, *ON*
Mike Evans, Toronto, *ON*
Keith Finnie, London, *ON*
Gerald Levine, Barrie, *ON*
Mitchell Levine, Hamilton, *ON* (Chair)
Christopher Morgan, Toronto, *ON*
David Massel, London, *ON*
Robert McKelvie, Hamilton, *ON*
Richard Ogilvie, Toronto, *ON*
Ashish Pradhan, Hamilton, *ON*
John Stewart, Port Perry, *ON*
Anna Woo, Toronto, *ON*

Corresponding stakeholders

AstraZeneca, Mississauga, *ON*
Bayer Inc, Toronto, *ON*
Bristol-Myers Squibb, Saint-Laurent, *QC*
Lawrence Burr, Vancouver, *BC*
DuPont Pharma, Mississauga, *ON*
Rudy Gasparelli, Wawa, *ON*
Barry Goldlist, Toronto, *ON*
Robert J. Howard, Toronto, *ON*
ICN Canada Ltd., Montreal, *QC*
Allen Huang, Montreal, *QC*
Chris MacKnight, Halifax, *NS*
Janice Menezes, Vancouver, *BC*
Merck-Frosst Inc, Kirkland, *QC*
Novartis, Dorval, *QC*
Blair O'Neil, Halifax, *NS*
Grahame Owen, Oakville, *ON*
Parke Davis, Toronto, *ON*
Pharmacia & Upjohn Inc, Don Mills, *ON*
Pfizer Canada Inc, Kirkland, *QC*
Val Rachlis, North York, *ON*
Irene Turpie, Hamilton, *ON*

The views expressed in this document may not be representative of the views held by some of the individual participants, nor the institutions or organizations that they are affiliated with. Development of these guidelines was completed March 2000.

Preamble

Purpose

This guideline has been devised in order to assist primary care physicians to use drugs optimally in the management of ischemic heart disease based on the best available evidence.

Guideline development process

The guideline development process combines critical assessment of available research evidence with expert clinical opinion of clinicians and researchers. The process is overseen by a Review Panel consisting of family physicians, relevant specialists, clinical pharmacologists, pharmacists and epidemiologists representing various regions of the province, academic and community-based clinical practice, and research. The process progresses through the following stages:

- Compilation, rigorous review and critical appraisal of evidence sources, including a thorough literature search for relevant trials, meta-analyses, practice guidelines and economic analyses.
- Preparation of a draft of the guidelines, including a grade assigned to each recommendation indicating the strength of its supporting evidence, with drugs designated "first-line" or other based on the strength of efficacy data, adverse effect profile, cost, availability, convenience and other factors.
- Review and comment by a broad spectrum of external stakeholders, including all relevant health care professionals, professional societies, pharmaceutical companies, the Ministry of Health and Long-Term Care, and consumers.
- Progressive refinement of the guidelines, and formulation in final form for publication, by the Review Panel, based on their assessment of the evidence and input from the stakeholder review.

Further details of the process used to develop this consensus guideline can be obtained by contacting OPOT at the following address:

Ontario Program for Optimal Therapeutics
708-25 Charlton Ave E
Hamilton, *ON*, L8N 1Y2

Drug costs

Costs are based on the prices stated in the Ontario drug benefit formulary / comparative price index, no. 36 (1999) and a survey of retail pharmacy wholesale acquisition costs.

Recommendation grades

The following scheme has been used to grade the strength of the recommendations made within the document.

Grade A: **Strong recommendation.** The recommendation is based primarily upon well-designed randomized controlled trials (RCT's) or meta-analyses that assure clinically important outcomes (i.e. mortality reduction).

Grade B: **Moderate recommendation.** The recommendation is a combination of high quality evidence and expert opinion.

Grade C: Weak recommendation. The recommendation is based principally upon expert opinion.

Acknowledgements

This 'Guidelines' package was funded by the Ontario Program of Optimal Therapeutics (OPOT) which is supported by a grant from the Ontario Ministry of Health.

Section I

Introduction

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Introduction

Background

Ischemic heart disease (IHD) was responsible for 56% of deaths related to cardiovascular disease and 21% of all deaths in Canada in 1995.[1] Optimum use of therapeutic technologies is highly effective in the primary and secondary prevention of mortality due to IHD.

Definition

Stable ischemic heart disease is defined as symptomatic or investigational evidence of coronary artery disease in the absence of acute complications of unstable angina or acute myocardial infarction.

Strategy

A two-part strategy is recommended. The first part deals with modification of risk factors predisposing to the development of coronary artery disease and the second part highlights the use of drug therapy.

I) Risk factor modification

Risk factors increase the probability of ischemic cardiac events.[2] The presence of multiple risk factors confers a magnified risk, which is multiplicative rather than merely additive.[3,4]

Recommendations for identified modifiable risk factors:

a) ***Obesity:*** Promote dietary measures to achieve ideal Body Mass Index, BMI= weight (kg) /height $(m)^2$. Refer to appendix C for nomogram.[5]

Body Mass Index	Inference
≥ 30	Obese
> 25 to 29.9	Overweight
20 to 25	***Ideal***

b) ***Physical inactivity:*** Encourage a moderate amount of exercise (e.g. a brisk walk) 30 to 60 minutes at least three times weekly up to but short of producing symptoms.

c) ***Smoking:*** Implement smoking cessation therapy using bupropion or a nicotine patch in conjunction with a counseling program. Patients need to identify a 'target quitting date' at commencement of bupropion therapy.[6,7] *Smoking cessation aids are safe for persons with ischemic heart disease.*

Introduction

Background

Ischemic heart disease (IHD) was responsible for 56% of deaths related to cardiovascular disease and 21% of all deaths in Canada in 1995. Optimum use of therapeutic technologies is highly effective in the primary and secondary prevention of mortality due to IHD.

Definition

Stable ischemic heart disease is defined as symptomatic or investigational evidence of coronary artery disease in the absence of acute complications of unstable angina or acute myocardial infarction.

Strategy

A two-part strategy is recommended. The first part deals with modification of risk factors predisposing to the development of coronary artery disease and the second part highlights the use of drug therapy.

I) Risk factor modification

Risk factors increase the probability of ischemic cardiac events.[1] The presence of multiple risk factors confers a magnified risk, which is multiplicative rather than merely additive.[1]

Recommendations for identified modifiable risk factors:

a) ***Obesity***: Promote dietary measures to achieve ideal Body Mass Index, BMI= weight (kg) / height (m)^2. Refer to appendix C for nomogram.

Body Mass Index	Inference
≥ 30	Obese
> 25 to 29.9	Overweight
20 to 25	***Ideal***

b) ***Physical inactivity***: Encourage a moderate amount of exercise (e.g. a brisk walk) 30 to 60 minutes at least three times weekly up to but short of producing symptoms.

c) ***Smoking***: Implement smoking cessation therapy using bupropion or a nicotine patch in conjunction with a counseling program. Patients need to identify a 'target quitting date' at commencement of bupropion therapy.[2] *Smoking cessation aids are safe for persons with ischemic heart disease.*

Smoking cessation aids	Recommended regimen		Total cost of therapy ($)
Bupropion SR (9 week regimen; recommended 'quit date' is the 8th day of therapy)	**Regimen**	**Dose**	100.00
	Day 1 - 3	150 mg o.d	
	Day 4 to the end of the 9th week	150 mg b.i.d	
Nicotine patch (to be applied starting on the 'quit date')	**Week**	**Dose**	200.00
	1-7	21 mg/day	
	8	14 mg/day	
	9	7 mg/day	

d) ***Diet:*** Refer to appendix B (*page 32*).

e) ***Diabetes mellitus*:** An isolated HbA_{1c} is the preferred outcome in evaluating risk, with the optimal level < 7%. Alternatively, recommended target fasting or preprandial blood glucose is between 4.0 – 7.0 mmol/L and target postprandial blood glucose is between 5.0 – 11.0 mmol/L.[8]

f) ***Hypertension*:** Treatment is recommended if-
(1) BP > 140/90 mm Hg,
(2) isolated systolic BP > 160 mm Hg or,
(3) diabetes and BP > 130/80mm Hg.

To achieve a blood pressure below these thresholds may require the use of 3 antihypertensive medications.

g) ***Dyslipidemia*:** Initiate therapy with HMG CoA reductase inhibitors if LDL-C is ≥ 3.0 mmol/L. LDL-C target level to be achieved is < 2.5 mmol/L.[7]

h) ***Hormone replacement therapy (HRT)*:** Use of HRT in women with IHD (secondary prevention) is controversial. If the patient has been on HRT for more than 2 years it is not necessary to stop therapy. Initiation of therapy is an individual decision, taking into consideration other health benefits.

i) ***Age*:** Treating the elderly may confer greater absolute benefits than for younger patients, because of a greater baseline risk with increasing age. Advancing age SHOULD NOT limit access to the use of appropriate therapy.

Smoking cessation aids	Recommended regimen		Total cost of therapy ($)
Bupropion SR (9 week regimen; recommended 'quit date' is the 8th day of therapy)	**Regimen**	**Dose**	100.00
	Day 1 - 3	150 mg o.d	
	Day 4 to the end of the 9th week	150 mg b.i.d	
Nicotine patch (to be applied starting on the 'quit date')	**Week**	**Dose**	200.00
	1-7	21 mg/day	
	8	14 mg/day	
	9	7 mg/day	

d) ***Diet:*** Refer to appendix B (*page 32*).

e) ***Diabetes mellitus*:** An isolated HbA_{1c} is the preferred outcome in evaluating risk, with the optimal level < 7%. Alternatively, recommended target fasting or preprandial blood glucose is between 4.0 – 7.0 mmol/L and target postprandial blood glucose is between 5.0 – 11.0 mmol/L.[8]

f) ***Hypertension*:** Treatment is recommended if-
(1) BP > 140/90 mm Hg,
(2) isolated systolic BP > 160 mm Hg or,
(3) diabetes and BP > 130/80mm Hg.

To achieve a blood pressure below these thresholds may require the use of 3 antihypertensive medications.

g) ***Dyslipidemia:*** Initiate therapy with HMG CoA reductase inhibitors if LDL-C is ≥ 3.0 mmol/L. LDL-C target level to be achieved is < 2.5 mmol/L.[9]

h) ***Hormone replacement therapy (HRT):*** Use of HRT in women with IHD (secondary prevention) is controversial. If the patient has been on HRT for more than 2 years it is not necessary to stop therapy. Initiation of therapy is an individual decision, taking into consideration other health benefits.

i) ***Age*:** Treating the elderly may confer greater absolute benefits than for younger patients, because of a greater baseline risk with increasing age. Advancing age SHOULD NOT limit access to the use of appropriate therapy.

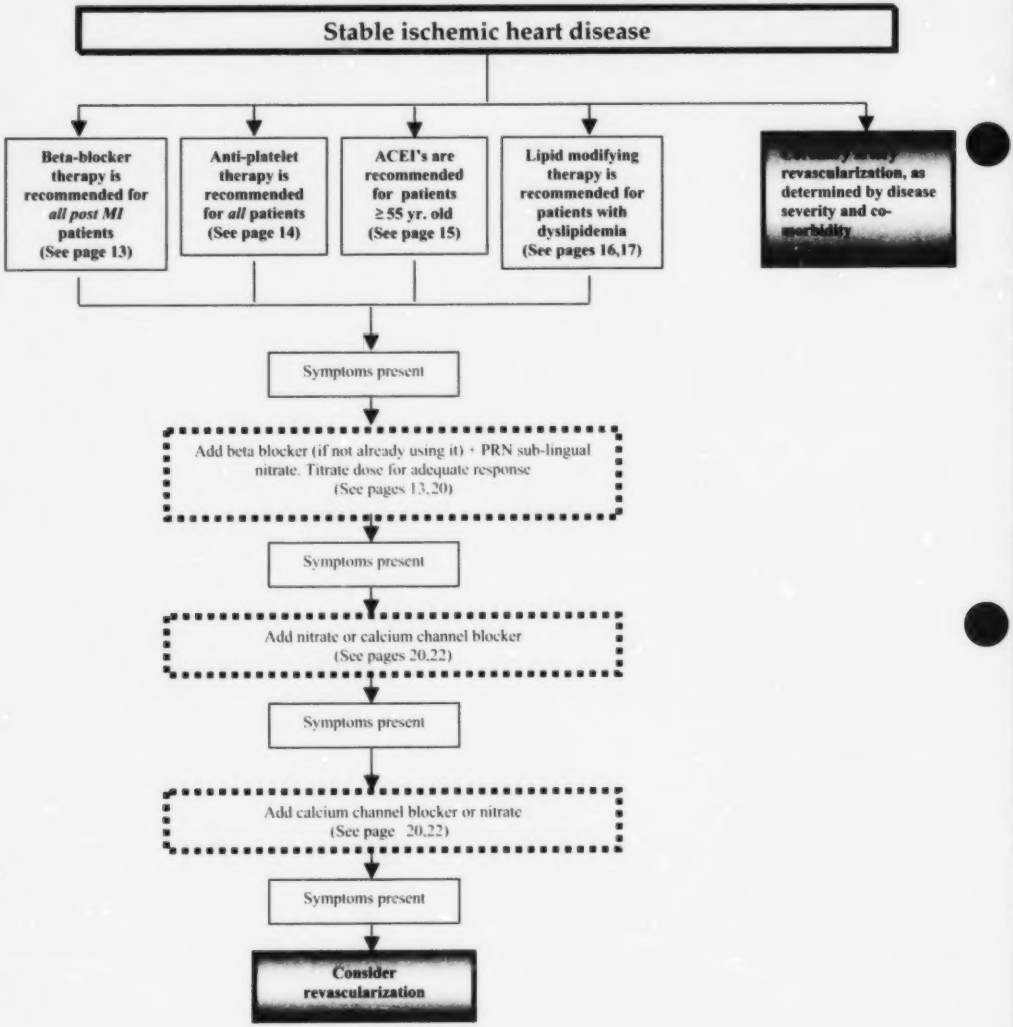
II) Use of drug therapy

There are two types of drugs that are recommended for use in the management of stable ischemic heart disease.

Disease modifying drugs have been found in randomized controlled trials to modify the course of ischemic heart disease and reduce mortality. Drugs belonging to this group are *beta-blockers, antiplatelet agents, ACE inhibitors* and *lipid modifying drugs.*

Symptom modifying drugs are used predominantly to modify the symptoms of ischemic heart disease. Drugs belonging to this group are *beta-blockers, nitrates* and *calcium channel blockers.*

Algorithm for using drug therapy for stable ischemic heart disease (IHD)


Stable ischemic heart disease
Beta-blocker therapy is recommended for *all post MI* patients (See page 13)
Anti-platelet therapy is recommended for *all* patients (See page 14)
ACEI's are recommended for patients ≥ 55 yr. old (See page 15)
Lipid modifying therapy is recommended for patients with dyslipidemia (See pages 16,17)
revascularization, as determined by disease severity and co-morbidity
Symptoms present
Add beta blocker (if not already using it) + PRN sub-lingual nitrate. Titrate dose for adequate response (See pages 13,20)
Symptoms present
Add nitrate or calcium channel blocker (See pages 20,22)
Symptoms present
Add calcium channel blocker or nitrate (See page 20,22)
Symptoms present
Consider revascularization
Disease modifying drug therapy procedure
Symptom modifying drug therapy
Disease or symptom modifying

Coexistence of modifiable risk factors such as *diabetes, hypertension, dyslipidemia* or *smoking* can lead to a multiplicative effect in occurrence of adverse cardiac outcomes. Risk factor modification can lead to a significant reduction in cardiac events.

Section II

Disease Modifying Therapy

Ontario Program for Optimal Therapeutics

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Disease modifying therapy

Beta-blockers [2,10]

Note: Long term use of beta-blockers has been shown to reduce mortality in symptomatic and asymptomatic post myocardial infarction (MI) patients. In general, beta-blockers should be continued indefinitely in all but low risk post-MI patients.

Recommendation

- Beta-blockers are effective therapy for all post- MI patients with chronic ischemic heart disease and systemic hypertension.
- Therapy is to be continued indefinitely once it has been initiated.
- Beta-blockers are contraindicated in patients with asthma and respiratory disorders that require a beta-agonist. They can be used in all patients with other respiratory diseases not requiring the use of a beta-agonist.
- In diabetics where a concern for hypoglycemia exists, cardioselective-selective blockers are preferred.
- In patients with peripheral vascular disease (PVD) use of a beta-blocker is recommended, recognizing that PVD symptoms may worsen while the risk of cardiac events will decline.

Grade of Recommendation: A (Strong recommendation)

Note: *The drugs in this class can be divided into two groups based on the availability of evidence.*
Group A*- Beta-blockers that have been extensively studied in the treatment of ischemic heart disease with respect to mortality.*
Group B*- Beta-blockers that have not been extensively studied in the treatment of ischemic heart disease with respect to mortality.*

Name	Dose	Daily cost ($)
Group A		
Cardioselective agents		
Atenolol	50 - 200 mg o.d	0.35 - 1.16
Metoprolol	25 - 100 mg b.i.d	0.12 - 0.44
Noncardioselective agents		
Propranolol	40 - 120 mg b.i.d	0.07 - 0.42
Timolol	10 - 20 mg b.i.d	0.50 - 1.00
Group B		
Cardioselective agent		
Acebutolol	100 - 400 mg b.i.d	0.33 - 0.97
Noncardioselective agent		
Nadolol	40 - 320 mg o.d	0.25 - 1.32

Sotalol should not be used for this indication.

See appendix A for common brand names in this class.

Disease modifying therapy

Beta-blockers [2,10]

Note: Long term use of beta-blockers has been shown to reduce mortality in symptomatic and asymptomatic post myocardial infarction (MI) patients. In general, beta-blockers should be continued indefinitely in all but low risk post-MI patients.

Recommendation

- Beta-blockers are effective therapy for all post- MI patients with chronic ischemic heart disease and systemic hypertension.
- Therapy is to be continued indefinitely once it has been initiated.
- Beta-blockers are contraindicated in patients with asthma and respiratory disorders that require a beta-agonist. They can be used in all patients with other respiratory diseases not requiring the use of a beta-agonist.
- In diabetics where a concern for hypoglycemia exists, cardioselective-selective blockers are preferred.
- In patients with peripheral vascular disease (PVD) use of a beta-blocker is recommended, recognizing that PVD symptoms may worsen while the risk of cardiac events will decline.

Grade of Recommendation: A (Strong recommendation)

Note: *The drugs in this class can be divided into two groups based on the availability of evidence.*
Group A*- Beta-blockers that have been extensively studied in the treatment of ischemic heart disease with respect to mortality.*
Group B*- Beta-blockers that have not been extensively studied in the treatment of ischemic heart disease with respect to mortality.*

Name	Dose	Daily cost ($)
Group A		
Cardioselective agents		
Atenolol	50 - 200 mg o.d	0.35 - 1.16
Metoprolol	25 - 100 mg b.i.d	0.12 - 0.44
Noncardioselective agents		
Propranolol	40 - 120 mg b.i.d	0.07 - 0.42
Timolol	10 - 20 mg b.i.d	0.50 - 1.00
Group B		
Cardioselective agent		
Acebutolol	100 - 400 mg b.i.d	0.33 - 0.97
Noncardioselective agent		
Nadolol	40 - 320 mg o.d	0.25 - 1.32

Sotalol should not be used for this indication.

See appendix A for common brand names in this class.

Anti-platelet and anti-thrombotic agents [2,11-14]

Note: Anti-platelet and anti-thrombotic therapy has been shown to reduce the incidence of all 'vascular events' in large randomized controlled trials.

Recommendation

- Anti-platelet therapy is recommended for all patients with chronic ischemic heart disease.
- Therapy is to be continued indefinitely.
- Acetyl Salicylic Acid (ASA) is the drug of choice because of proven efficacy.
- Ticlopidine and clopidogrel are appropriate alternatives to ASA in patients intolerant to ASA.
- Clopidogrel probably has less major toxicity than ticlopidine but is more expensive.
- Warfarin has been shown to be efficacious and may be used in patients with concomitant atrial fibrillation (optimal target INR: 2 – 3).

Grade of Recommendation: A (Strong recommendation)

Efficacy of ASA has been demonstrated over a wide range of doses, as low as 80 mg/day.

Name	Dose	Daily cost ($)
ASA	325 mg o.d	0.02
ASA	81 mg o.d	0.13
Clopidogrel	75 mg o.d	3.29
Ticlopidine	250 mg o.d	0.81
Warfarin	INR: 2-3	0.28 - 0.37

See appendix A for common brand names in this class.

ACE inhibitors [15]

Note: ACE inhibitor therapy has been shown to reduce the incidence of all 'vascular events' in a large randomized controlled trial. Ramipril has been the best studied drug in this class for this condition.

Recommendation

- ACE inhibitor therapy is recommended for patients ≥ 55 yr. old with stable ischemic heart disease.
- Therapy should be continued for a minimum of 5 years.

Grade of Recommendation: A (Strong recommendation)

Note:
The drugs in this class can be divided into two groups based on the availability of evidence.
Group A*- ACEI's that have been extensively studied in the treatment of ischemic heart disease (normal or abnormal left ventricular dysfunction) with respect to mortality.*
Group B*- ACEI's that have not been extensively studied in the treatment of ischemic heart disease with respect to mortality.*

Name	Dose	Daily cost ($)
	Group A	
Captopril	6.25 - 50 mg t.i.d	0.64 - 1.68
Enalapril	2.5 - 20 mg b.i.d	0.68 - 2.32
Lisinopril	2.5 - 30 mg o.d	0.34 - 1.78
Ramipril	2.5 - 10 mg o.d	0.75 - 0.95
Trandolapril	1 - 4 mg o.d	0.67 - 1.54
	Group B	
Benazepril	10 - 40 mg o.d	0.68 - 1.56
Cilazapril	0.5 - 5 mg o.d	0.60 - 0.79
Fosinopril	5 - 40 mg o.d	0.40 -1.90
Perindopril	4 - 8 mg o.d	0.75 -1.50
Quinapril	10 - 40 mg o.d	0.82 - 0.82

See appendix A for common brand names in this class.

Anti-platelet and anti-thrombotic agents [2,11-14]

Note: Anti-platelet and anti-thrombotic therapy has been shown to reduce the incidence of all 'vascular events' in large randomized controlled trials.

Recommendation

- Anti-platelet therapy is recommended for all patients with chronic ischemic heart disease.
- Therapy is to be continued indefinitely.
- Acetyl Salicylic Acid (ASA) is the drug of choice because of proven efficacy.
- Ticlopidine and clopidogrel are appropriate alternatives to ASA in patients intolerant to ASA.
- Clopidogrel probably has less major toxicity than ticlopidine but is more expensive.
- Warfarin has been shown to be efficacious and may be used in patients with concomitant atrial fibrillation (optimal target INR: 2 – 3).

Grade of Recommendation: A (Strong recommendation)

Efficacy of ASA has been demonstrated over a wide range of doses, as low as 80 mg/day.

Name	Dose	Daily cost ($)
ASA	325 mg o.d	0.02
ASA	81 mg o.d	0.13
Clopidogrel	75 mg o.d	3.29
Ticlopidine	250 mg o.d	0.81
Warfarin	INR: 2-3	0.28 - 0.37

See appendix A for common brand names in this class.

ACE inhibitors [15]

Note: ACE inhibitor therapy has been shown to reduce the incidence of all 'vascular events' in a large randomized controlled trial. Ramipril has been the best studied drug in this class for this condition.

Recommendation

- ACE inhibitor therapy is recommended for patients ≥ 55 yr. old with stable ischemic heart disease.
- Therapy should be continued for a minimum of 5 years.

Grade of Recommendation: A (Strong recommendation)

Note:
The drugs in this class can be divided into two groups based on the availability of evidence.
Group A*- ACEI's that have been extensively studied in the treatment of ischemic heart disease (normal or abnormal left ventricular dysfunction) with respect to mortality.*
Group B*- ACEI's that have not been extensively studied in the treatment of ischemic heart disease with respect to mortality.*

Name	Dose	Daily cost ($)
	Group A	
Captopril	6.25 - 50 mg t.i.d	0.64 - 1.68
Enalapril	2.5 - 20 mg b.i.d	0.68 - 2.32
Lisinopril	2.5 - 30 mg o.d	0.34 - 1.78
Ramipril	2.5 - 10 mg o.d	0.75 - 0.95
Trandolapril	1 - 4 mg o.d	0.67 - 1.54
	Group B	
Benazepril	10 - 40 mg o.d	0.68 - 1.56
Cilazapril	0.5 - 5 mg o.d	0.60 - 0.79
Fosinopril	5 - 40 mg o.d	0.40 -1.90
Perindopril	4 - 8 mg o.d	0.75 -1.50
Quinapril	10 - 40 mg o.d	0.82 - 0.82

See appendix A for common brand names in this class.

Lipid modifying therapy [2,9,16-18]

Note: Reduction of serum cholesterol levels with HMG-CoA reductase inhibitors ('statins') has been shown to reduce mortality in patients with ischemic heart disease. There is a direct relationship between the reduction of serum cholesterol levels and decrease in the risk of ischemic events.

Recommendation

- HMG-CoA reductase inhibitors are recommended in patients with chronic ischemic heart disease in patients who have a serum LDL-C ≥ 3.0 mmol/L. Titrate doses to achieve target lipid levels (LDL-C < 2.5 mmol/L).
- Gemfibrozil (fibrates) can be used in patients with low HDL-C (< 1.0 mmol/L), and low levels of LDL-C (= 3.0 mmol/L), total cholesterol (= 4.5 mmol/L) and moderate levels of triglycerides (= 2.0 mmol/L).
- Therapy is to be continued for a minimum of 5 years. Therapeutic results beyond 5 years are less certain but longer therapy is probably beneficial.

Grade of Recommendation: A (Strong recommendation)

HMG-CoA reductase inhibitors (Statins)

Note:
The drugs in this class can be divided into two groups based on the availability of evidence.
Group A- Statins that *have shown a reduction in cardiovascular event rates* in large scale randomized controlled trials.
Group B- Statins that *have not been tested for cardiac end-points* in large scale randomized controlled trials.

Name	Dose	Daily cost ($)
	Group A	
Lovastatin	20 – 40 mg o.d	1.30 - 2.40
Pravastatin	10 – 40 mg o.d	1.51 - 2.15
Simvastatin	5 – 80 mg o.d	0.90 - 4.40
	Group B	
Atorvastatin	10 – 40 mg o.d	1.60 - 2.15
Cerivastatin	0.2 – 0.4 mg o.d	1.20 - 1.60
Fluvastatin	20 – 80 mg o.d	0.75 - 2.10

See appendix A for common brand names in this class.

Fibrates

Note:
The drugs in this class can be divided into two groups based on the availability of evidence.
Group A- Fibrate that *has shown a reduction in cardiovascular event rates* in large scale randomized controlled trials.
Group B- Fibrates that *have not been tested for cardiac end points* in large scale randomized controlled trials.

Name	Dose	Daily cost ($)
	Group A	
Gemfibrozil	600 mg b.i.d	1.39
	Group B	
Bezafibrate	200 mg t.i.d	2.64
	400 mg SR o.d	1.60
Fenofibrate	100 mg t.i.d	1.29
	200 mg cap o.d	1.73

See appendix A for common brand names in this class.

Lipid modifying therapy [2,9,16-18]

Note: Reduction of serum cholesterol levels with HMG-CoA reductase inhibitors ('statins') has been shown to reduce mortality in patients with ischemic heart disease. There is a direct relationship between the reduction of serum cholesterol levels and decrease in the risk of ischemic events.

Recommendation

- HMG-CoA reductase inhibitors are recommended in patients with chronic ischemic heart disease in patients who have a serum LDL-C ≥ 3.0 mmol/L. Titrate doses to achieve target lipid levels (LDL-C < 2.5 mmol/L).
- Gemfibrozil (fibrates) can be used in patients with low HDL-C (< 1.0 mmol/L), and low levels of LDL-C (= 3.0 mmol/L), total cholesterol (= 4.5 mmol/L) and moderate levels of triglycerides (= 2.0 mmol/L).
- Therapy is to be continued for a minimum of 5 years. Therapeutic results beyond 5 years are less certain but longer therapy is probably beneficial.

Grade of Recommendation: A (Strong recommendation)

HMG-CoA reductase inhibitors (Statins)

Note:
The drugs in this class can be divided into two groups based on the availability of evidence.
Group A- Statins that *have shown a reduction in cardiovascular event rates* in large scale randomized controlled trials.
Group B- Statins that *have not been tested for cardiac end-points* in large scale randomized controlled trials.

Name	Dose	Daily cost ($)
	Group A	
Lovastatin	20 – 40 mg o.d	1.30 - 2.40
Pravastatin	10 – 40 mg o.d	1.51 - 2.15
Simvastatin	5 – 80 mg o.d	0.90 - 4.40
	Group B	
Atorvastatin	10 – 40 mg o.d	1.60 - 2.15
Cerivastatin	0.2 – 0.4 mg o.d	1.20 - 1.60
Fluvastatin	20 – 80 mg o.d	0.75 - 2.10

See appendix A for common brand names in this class.

Fibrates

Note:
The drugs in this class can be divided into two groups based on the availability of evidence.
Group A- Fibrate that *has shown a reduction in cardiovascular event rates* in large scale randomized controlled trials.
Group B- Fibrates that *have not been tested for cardiac end points* in large scale randomized controlled trials.

Name	Dose	Daily cost ($)
	Group A	
Gemfibrozil	600 mg b.i.d	1.39
	Group B	
Bezafibrate	200 mg t.i.d	2.64
	400 mg SR o.d	1.60
Fenofibrate	100 mg t.i.d	1.29
	200 mg cap o.d	1.73

See appendix A for common brand names in this class.

Section III

Symptom Modifying Therapy

Ontario Program for Optimal Therapeutics

Symptom modifying therapy

Nitrate therapy [2,19]

Note: At present there is no evidence to indicate a mortality benefit from the long-term use of nitrates in patients with ischemic heart disease.

Recommendation

- Nitrates are to be used for the symptomatic relief of anginal pain as well as for symptom prophylaxis.
- Nitrates in the form of sprays or sub-lingual tablets can be used for acute symptom management. Sprays and tablets are considered equally effective.
- Isosorbide dinitrate is the preferred drug for oral consumption as there are no clinically important differences amongst available formulations.
- Titrate the nitrate dose for optimum response.
- Oral nitrate preparations can be given three times daily with a minimum 14-h period of no drug administration in each 24-h cycle to prevent tolerance.
- Nitrate patches can be applied daily with a minimum 12-h period of no drug administration in each 24-h cycle to prevent tolerance.
- Timing of therapy should be individualized to maximize symptom management.

Grade of Recommendation: A (Strong recommendation)

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Name (formulation)	Route	Dose	Daily cost ($)
Treatment			
Nitroglycerin (tab)	SL	0.3 to 0.6 mg, 1 to 3 times*	0.03 - 0.09
Nitroglycerin (spray)	SL	0.4 to 0.8 mg, 1 to 3 times*	0.06 - 0.12
Nitroglycerin (tab)	Buccal	1 to 3 mg 1 time	0.22 - 0.30
Prophylaxis			
Nitroglycerin (tab)	SL	0.3 to 0.6 mg 2 to 5 min before activity	0.03 - 0.09
Nitroglycerin (spray)	SL	0.4 to 0.8 mg 2 to 5 min before activity	0.06 - 0.12
Nitroglycerin (tab)	Buccal	1 to 3 mg 3 times daily, tablet removed overnight	0.66 - 0.90
Nitroglycerin ERF**	Oral	2.6 to 10.4 mg 1 to 2 times daily	0.38 - 3.04
Nitroglycerin (Ointment)	Transdermal	1 to 2 inches / day remove for 12 h	0.21 - 0.42
Nitroglycerin (patch)	Transdermal	0.2 to 0.8 mg/h 1 time daily, 12h patch free interval	0.64 - 0.64
ISDN ERF**	SL	2.5 to 10 mg 5 to 10 min. before activity	0.05 - 0.07
ISDN	Oral	10 to 45 mg 3 times daily, 12 h tablet-free interval	0.02 - 0.26
ISDN ERF**	Oral	20 to 80 mg 1 to 2 times daily	0.35 - 2.80
IS-5-MN	Oral	10 to 20 mg 2 times daily, 7 h between doses	0.25 - 1.00
IS-5-MN ERF**	Oral	30 to 240 mg 1 time daily	0.39 - 3.12

* May be repeated after 5 min for a total of three doses. If pain persists, patient should seek medical attention; ** ERF- Extended Release Formulation.

See appendix A for common brand names in this class.

Name (formulation)	Route	Dose	Daily cost ($)
		Treatment	
Nitroglycerin (tab)	SL	0.3 to 0.6 mg, 1 to 3 times*	0.03 - 0.09
Nitroglycerin (spray)	SL	0.4 to 0.8 mg, 1 to 3 times*	0.06 - 0.12
Nitroglycerin (tab)	Buccal	1 to 3 mg 1 time	0.22 - 0.30
		Prophylaxis	
Nitroglycerin (tab)	SL	0.3 to 0.6 mg 2 to 5 min before activity	0.03 - 0.09
Nitroglycerin (spray)	SL	0.4 to 0.8 mg 2 to 5 min before activity	0.06 - 0.12
Nitroglycerin (tab)	Buccal	1 to 3 mg 3 times daily, tablet removed overnight	0.66 - 0.90
Nitroglycerin ERF**	Oral	2.6 to 10.4 mg 1 to 2 times daily	0.38 - 3.04
Nitroglycerin (Ointment)	Transdermal	1 to 2 inches / day remove for 12 h	0.21 - 0.42
Nitroglycerin (patch)	Transdermal	0.2 to 0.8 mg/h 1 time daily, 12h patch free interval	0.64 - 0.64
ISDN ERF**	SL	2.5 to 10 mg 5 to 10 min. before activity	0.05 - 0.07
ISDN	Oral	10 to 45 mg 3 times daily, 12 h tablet-free interval	0.02 - 0.26
ISDN ERF**	Oral	20 to 80 mg 1 to 2 times daily	0.35 - 2.80
IS-5-MN	Oral	10 to 20 mg 2 times daily, 7 h between doses	0.25 - 1.00
IS-5-MN ERF**	Oral	30 to 240 mg 1 time daily	0.39 - 3.12

* May be repeated after 5 min for a total of three doses. If pain persists, patient should seek medical attention; ** ERF- Extended Release Formulation.

See appendix A for common brand names in this class.

Calcium channel blockers [2,20-24]

Note: Nifedipine capsules with immediate release kinetics are NOT recommended as monotherapy in the treatment of chronic stable angina as it may lead to an increased risk of cardiovascular events. Mortality benefit with the use of CCB's has not been demonstrated in large clinical trials.

Recommendation

- Calcium channel blockers (CCB's) are recommended for use in patients intolerant or unresponsive to both nitrate AND beta-blocker therapy.
- A long acting dihydropyridine CCB can be administered to patients having signs and symptoms of myocardial ischemia while receiving optimal doses of beta-blocker therapy.
- Heart rate reducing CCB's (Verapamil, Diltiazem) can be used in the post-MI setting if there is no evidence of left ventricular dysfunction.
- Amlodipine can be used with caution in patients with left ventricular dysfunction. Verapamil or diltiazem should be avoided in patients with left ventricular dysfunction.
- Patients not using a beta-blocker should use rate limiting CCB's.
- Long acting CCB's may be used in hypertensive patients with angina.

Grade of Recommendation: C (Weak recommendation)

Name	Dose	Daily cost ($)
Long acting dihydropyridines		
Amlodipine	10 mg o.d	1.90
Nifedipine ERF*	20 - 60 mg o.d	0.75 - 1.46
Nifedipine ERF*	40 mg b.i.d	1.56
Rate reducing CCB's		
Diltiazem	30 - 60 mg q.i.d	0.83 - 1.45
Diltiazem ERF*	60 - 180 mg b.i.d	0.72 - 2.18
Diltiazem ERF*	180 - 360 mg o.d	1.07 - 2.15
Verapamil	80 - 120 mg t.i.d	0.85 - 1.28
Verapamil ERF*	240 - 360 mg o.d	0.87 - 1.30

*ERF- Extended Release Formulation

See appendix A for common brand names in this class.

Calcium channel blockers [2,20-24]

Note: Nifedipine capsules with immediate release kinetics are NOT recommended as monotherapy in the treatment of chronic stable angina as it may lead to an increased risk of cardiovascular events. Mortality benefit with the use of CCB's has not been demonstrated in large clinical trials.

Recommendation

- Calcium channel blockers (CCB's) are recommended for use in patients intolerant or unresponsive to both nitrate AND beta-blocker therapy.
- A long acting dihydropyridine CCB can be administered to patients having signs and symptoms of myocardial ischemia while receiving optimal doses of beta-blocker therapy.
- Heart rate reducing CCB's (Verapamil, Diltiazem) can be used in the post-MI setting if there is no evidence of left ventricular dysfunction.
- Amlodipine can be used with caution in patients with left ventricular dysfunction. Verapamil or diltiazem should be avoided in patients with left ventricular dysfunction.
- Patients not using a beta-blocker should use rate limiting CCB's.
- Long acting CCB's may be used in hypertensive patients with angina.

Grade of Recommendation: C (Weak recommendation)

Name	Dose	Daily cost ($)
	Long acting dihydropyridines	
Amlodipine	10 mg o.d	1.90
Nifedipine ERF*	20 - 60 mg o.d	0.75 - 1.46
Nifedipine ERF*	40 mg b.i.d	1.56
	Rate reducing CCB's	
Diltiazem	30 - 60 mg q.i.d	0.83 - 1.45
Diltiazem ERF*	60 - 180 mg b.i.d	0.72 - 2.18
Diltiazem ERF*	180 - 360 mg o.d	1.07 - 2.15
Verapamil	80 - 120 mg t.i.d	0.85 - 1.28
Verapamil ERF*	240 - 360 mg o.d	0.87 - 1.30

*ERF- Extended Release Formulation

See appendix A for common brand names in this class.

Reference List

Ontario Program for Optimal Therapeutics

References

1. Health Protection Branch, Laboratory Centre for Disease Control. Statistics Canada, 1997.
2. **CCS Consensus Conference on Chronic Ischemic Heart Disease.** *Can J Cardiol.* 1998; Vol. 14 Suppl C: 2C-23C.
3. **Evidence Based Cardiology.** Edited by Yusuf S et al. BMJ Books 1998. Pg 158-159.
4. Stamler J, Dyer A, Shekelle R, et al. **Relationship of baseline major risk factors to coronary and all-cause mortality, and to longevity: findings from long term follow-up of Chicago cohorts.** *Cardiol.* 1993; 82: 191-222.
5. **Executive Summary of the Clinical Guidelines on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults.** *Arch Intern Med.* 1998; 158: 1855-1867.
6. Hurt R, Sachs D, Glover E, et al. **A comparison of sustained-release bupropion and placebo for smoking cessation.** *NEJM.* 1997; 337: 1195-202.
7. Jorenby D, Leischow S, Nides M, et al. **A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation.** *NEJM.* 1999.; 340: 685-91.
8. Meltzer S, Leiter L, Daneman D, Gerstein H. **Clinical Practice Guidelines for the Management of Diabetes in Canada.** *CMAJ.* 1998; 159 (8 Suppl): S1-S29.
9. Frohlich J, Fodor G, McPherson R, et al for the Dyslipidemia Working Group of Health Canada. *Can J Cardiol.* 1998; 14(Suppl A): 17A-21A.
10. **The Beta-Blocker Pooling Project Research Group.** *Euro Heart J.* 1988; (9): 8-16.
11. Antiplatelet Trialists' Collaboration. Collaborative overview of randomized trials of anti-platelet therapy- I: **Prevention of death, myocardial infarction, and stroke by prolonged antiplatelet therapy in various categories of patients.** *BMJ.* 1994; 308: 81-106.
12. CAPRIE Steering Committee. **A randomized, blinded, trial of clopidogrel versus of aspirin in patients at risk of ischemic events (CAPRIE).** *Lancet.* 1996; 348: 1329-39.
13. Hirsh J, Dalen J, Anderson D, et al. **Oral anticoagulants- Mechanism of action, clinical effectiveness and optimal therapeutic range.** *Chest.* 1998; 114: 445S – 469S.
14. Laupacis A, Albers G, Dalen J, et al. **Antithrombotic therapy in atrial fibrillation.** *Chest.* 1995; 108(4): 352S-359S.
15. The Heart Outcomes Prevention Evaluation Study Investigators. **Effects of an Angiotensin-converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients.** *NEJM.* 2000; 342: 145-53.
16. Gould L, Rossouw J, Santanello N, Heyse J and Furberg C. **Cholesterol Reduction Yields Clinical Benefit- Impact of Statin Trials.** *Circulation.* 1998; 97: 946-952.
17. Scandinavian Simvastatin Survival Study Group. **Randomized trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S).** *Lancet.* 1994; 344: 1383-89.

18. Rubins H, Robins S, Collins D, et al., for the veterans affairs high-density lipoprotein cholesterol intervention trial study group. **Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol.** *NEJM.* 1999; 341: 410-418.
19. Holbrook A Dolovich L, Grootendorst P, et al. **Efficacy, Effectiveness and Cost Analysis of Nitrate Therapy for the Prevention of Angina Pectoris.** *Ottawa: Canadian Coordinating Office for Health Technology Assessment (CCOHTA);* August 1996.
20. Statson W, Schmid C, Niedzwiecki A, et al. **Safety of nifedipine in angina pectoris- A meta analysis.** *Hypertension.* 1999; 33: 24-31.
21. Rehnqvist N, Hjemdahl P, Billing E, et al. **The Angina Prognosis Study in Stockholm (APSIS).** *Euro Heart J.* 1996; 17: 76-81.
22. Dargie H, Ford I, Fox K, et al., on behalf of the TIBET Group. **Total Ischemic Burden European Trial (TIBET).** *Euro Heart J.* 1996; 17: 104-12.
23. Dunselman P, Liem A, Verdel G, et al. **Results of the Felodipine ER and Metoprolol CR in Angina (FEMINA) Study.** *Euro Heart J.* 1997; 18: 1755-1764.
24. Waters D. **Calcium channel blockers: An evidence-based review**. *Can J Cardiol.* 1997; 13(8): 757-766.
25. Eikelbloom J, Lonn E, Genest J, et al. **Homocysteine and cardiovascular risk: a critical review of the epidemiologic evidence.** *Ann Intern Med.* 1999; 131: 363-375.
26. Wald N, Watt H, Law M, Weir D, Mc Partlin J, Scott J. **Homocysteine and Ischemic Heart Disease- Results of a Prospective Study with Implications Regarding Prevention.** *Arch Intern Med.* 1998; 158: 862-867.
27. Homocysteine Lowering Trialists' Collaboration. **Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomized trials.** *BMJ.* 1998; 316: 894-898.

Appendices

Ontario Program for Optimal Therapeutics

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Appendices

Appendix A

Commonly Used Brand Names Corresponding to Generic Drug Names

Smoking cessation aids

Generic name	Trade names
Bupropion	*Zyban*
Nicotine patch	*Habitrol, Nicoderm, Nicotrol*

Beta-blockers

Generic name	Trade names
Group A	
Cardioselective agents	
Atenolol	*Apo-Atenolol, Gen-Atenolol, Novo-Atenolol, Nu-Atenolol, PMS-Atenolol, Rho-Atenolol, Scheinpharm Atenolol, Tenolin, Tenormin*
Metoprolol	*Apo-Metoprolol, Apometoprolol (Type L), Betaloc, Betaloc Durules, Lopressor, Novo-Metoprolol, Nu-Metop, PMS-Metoprolol-B, PMS-Metoprolol-L*
Noncardioselective agents	
Propranolol	*Apo-Propranolol, Inderal, Inderal-LA, Nu-Propranolol*
Timolol	*Apo-Timol, Blocadren, Novo-Timol, Nu-Timolol*
Group B	
Cardioselective agents	
Acebutolol	*Apo-Acebutolol, Monitan, Novo-Acebutolol, Nu-Acebutolol, Rhotral, Sectral*
Noncardioselectice agents	
Nadolol	*Alti-Nadolol, Apo-Nadolol, Corgard, Novo-Nadolol*

Anti-platelet and anti-thrombotic agents

Generic name	Trade names
ASA	*Apo-ASA, Entrophen, Novasen, MSD Enteric Coated ASA*
Clopidogrel	*Plavix*
Ticlopidine	*Apo-Ticlopidine, Nu-Ticlopidine, Ticlid*
Warfarin	*Coumadin*

Appendices

Appendix A

Commonly Used Brand Names Corresponding to Generic Drug Names

Smoking cessation aids

Generic name	Trade names
Bupropion	*Zyban*
Nicotine patch	*Habitrol, Nicoderm, Nicotrol*

Beta-blockers

Generic name	Trade names
Group A	
Cardioselective agents	
Atenolol	*Apo-Atenolol, Gen-Atenolol, Novo-Atenolol, Nu-Atenolol, PMS-Atenolol, Rho-Atenolol, Scheinpharm Atenolol, Tenolin, Tenormin*
Metoprolol	*Apo-Metoprolol, Apometoprolol (Type L), Betaloc, Betaloc Durules, Lopressor, Novo-Metoprolol, Nu-Metop, PMS-Metoprolol-B, PMS-Metoprolol-L*
Noncardioselective agents	
Propranolol	*Apo-Propranolol, Inderal, Inderal-LA, Nu-Propranolol*
Timolol	*Apo-Timol, Blocadren, Novo-Timol, Nu-Timolol*
Group B	
Cardioselective agents	
Acebutolol	*Apo-Acebutolol, Monitan, Novo-Acebutolol, Nu-Acebutolol, Rhotral, Sectral*
Noncardioselectice agents	
Nadolol	*Alti-Nadolol, Apo-Nadolol, Corgard, Novo-Nadolol*

Anti-platelet and anti-thrombotic agents

Generic name	Trade names
ASA	*Apo-ASA, Entrophen, Novasen, MSD Enteric Coated ASA*
Clopidogrel	*Plavix*
Ticlopidine	*Apo-Ticlopidine, Nu-Ticlopidine, Ticlid*
Warfarin	*Coumadin*

ACE inhibitors

Generic name	Trade names
Group A	
Captopril	*Apo-Capto, Capoten, Captril, Gen-Captopril, Novo- Captopril, Nu-Capto, PMS-Captopril*
Enalapril	*Vasotec*
Lisinopril	*Apo-Lisinopril, Prinivil, Zestril*
Ramipril	*Altace*
Trandolapril	*Mavik*
Group B	
Benazepril	*Lotensin*
Cilazapril	*Inhibace*
Fosinopril	*Monopril*
Perindopril	*Coversyl*
Quinapril	*Accupril*

HMG-CoA reductase inhibitors (Statins)

Generic name	Trade names
Group A	
Lovastatin	*Apo-Lovastatin, Mevacor*
Pravastatin	*Pravachol*
Simvastatin	*Zocor*
Group B	
Atorvastatin	*Lipitor*
Cerivastatin	*Baycol*
Fluvastatin	*Lescol*

Fibrates

Generic name	Trade names
Group A	
Gemfibrozil	*Apo-Gemfibrozil, Gemfibrozil, Gen-Gemfibrozil, Lopid*
Group B	
Bezafibrate	*Bezalip*
Fenofibrate	*Apo-Fenofibrate, Apo-Feno-Micro, Lipidil, Lipidil Micro, Nu-Fenofibrate*

Nitrate formulations

Generic name	Trade names
Nitroglycerin (tab)	*Nitrostat*
Nitroglycerin (tab) ERF*	*Nitrong SR*
Nitroglycerin (spray)	*Nitrolingual spray , Nitrolingual pumpspray*
Nitroglycerin (Ointment)	*Nitrol*
Nitroglycerin (patch)	*Trinipatch, Nitro-Dur, Minitran, Transderm Nitro*
ISDN	*Apo-ISDN, Isordil*
ISDN ERF*	*Cedocard SR*
IS-5-MN	*Ismo*
IS-5-MN ERF*	*Imdur*

*ERF- Extended Release Formulation

Calcium channel blockers

Generic name	Trade names
Long acting dihydropyridines	
Amlodipine	*Norvasc*
Nifedipine ERF*	*Apo-Nifed PA, Adalat PA 10, Adalat PA 20, Nu-Nifedipine PA, Schein Nifedipine PA*
Nifedipine ERF**	*Adalat XL*
Rate reducing CCB's	
Diltiazem	*Alti-Diltiazem, Apo-Diltiaz, Cardizem, Diltiazem, Gen-Diltiazem, Novo-Diltiazem, Nu-Diltiaz, Syn-Diltiazem*
Diltiazem ERF*	*Apo-Diltiaz SR, Cardizem SR, Gen-Diltiazem SR, Novo-Diltiazem SR*
Diltiazem ERF**	*Alti-Diltiazem CD, Apo-Diltiaz CD, Alti-Diltiazem CD, Cardizem CD, Nu-Diltiaz CD, Tiazac ER*
Verapamil	*Alti-Verapamil, Apo-Verap, Isoptin, Novo-Veramil, Nu-Verap, Verapamil*
Verapamil ERF**	*Chronovera, Gen-Verapamil SR, Isoptin SR, Novo-Veramil SR, Verelan*

*ERF- Extended Release Formulation; **ERF – Extended Release Formulation, once a day administration.

ACE inhibitors

Generic name	Trade names
Group A	
Captopril	*Apo-Capto, Capoten, Captril, Gen-Captopril, Novo- Captopril, Nu-Capto, PMS-Captopril*
Enalapril	*Vasotec*
Lisinopril	*Apo-Lisinopril, Prinivil, Zestril*
Ramipril	*Altace*
Trandolapril	*Mavik*
Group B	
Benazepril	*Lotensin*
Cilazapril	*Inhibace*
Fosinopril	*Monopril*
Perindopril	*Coversyl*
Quinapril	*Accupril*

HMG-CoA reductase inhibitors (Statins)

Generic name	Trade names
Group A	
Lovastatin	*Apo-Lovastatin, Mevacor*
Pravastatin	*Pravachol*
Simvastatin	*Zocor*
Group B	
Atorvastatin	*Lipitor*
Cerivastatin	*Baycol*
Fluvastatin	*Lescol*

Fibrates

Generic name	Trade names
Group A	
Gemfibrozil	*Apo-Gemfibrozil, Gemfibrozil, Gen-Gemfibrozil, Lopid*
Group B	
Bezafibrate	*Bezalip*
Fenofibrate	*Apo-Fenofibrate, Apo-Feno-Micro, Lipidil, Lipidil Micro, Nu-Fenofibrate*

Nitrate formulations

Generic name	Trade names
Nitroglycerin (tab)	*Nitrostat*
Nitroglycerin (tab) ERF*	*Nitrong SR*
Nitroglycerin (spray)	*Nitrolingual spray , Nitrolingual pumpspray*
Nitroglycerin (Ointment)	*Nitrol*
Nitroglycerin (patch)	*Trinipatch, Nitro-Dur, Minitran, Transderm Nitro*
ISDN	*Apo-ISDN, Isordil*
ISDN ERF*	*Cedocard SR*
IS-5-MN	*Ismo*
IS-5-MN ERF*	*Imdur*

*ERF- Extended Release Formulation

Calcium channel blockers

Generic name	Trade names
Long acting dihydropyridines	
Amlodipine	*Norvasc*
Nifedipine ERF*	*Apo-Nifed PA, Adalat PA 10, Adalat PA 20, Nu-Nifedipine PA, Schein Nifedipine PA*
Nifedipine ERF**	*Adalat XL*
Rate reducing CCB's	
Diltiazem	*Alti-Diltiazem, Apo-Diltiaz, Cardizem, Diltiazem, Gen-Diltiazem, Novo-Diltiazem, Nu-Diltiaz, Syn-Diltiazem*
Diltiazem ERF*	*Apo-Diltiaz SR, Cardizem SR, Gen-Diltiazem SR, Novo-Diltiazem SR*
Diltiazem ERF**	*Alti-Diltiazem CD, Apo-Diltiaz CD, Alti-Diltiazem CD, Cardizem CD, Nu-Diltiaz CD, Tiazac ER*
Verapamil	*Alti-Verapamil, Apo-Verap, Isoptin, Novo-Veramil, Nu-Verap, Verapamil*
Verapamil ERF**	*Chronovera, Gen-Verapamil SR, Isoptin SR, Novo-Veramil SR, Verelan*

*ERF- Extended Release Formulation; **ERF – Extended Release Formulation, once a day administration.

Appendix B

Investigational and unproven therapies

Mediterranean diet [2]

Recommendation

- A low saturated fat and high fibre diet offers relative protection.

Grade of Recommendation: B (Moderate recommendation)

Multi-vitamin supplementation [25-27]

Note: Observational data suggest a strong and sustained relationship between elevated plasma homocysteine levels and increased risk of cardiovascular disease in high risk populations. At present no randomized trials exist which demonstrate a reduction in cardiac events with folic acid intervention.

Recommendation

- Folic acid supplementation reduces the homocysteine levels within 2-6 weeks of initiating therapy. Mean dose- 0.4 mg/ day.
- Vitamin B_{12} in a dose of 400 to 1000 µg/ day could provide additional benefit.

Grade of Recommendation: C (Weak recommendation)

Anti-oxidant vitamin therapy [15]

Note: RCT evidence has demonstrated that anti-oxidant therapy with vitamin E has no benefit on cardiac event rates.

Recommendation

- Vitamin E as anti-oxidant therapy is **NOT** recommended to IHD patients.

Grade of Recommendation: A (Strong recommendation)

Chelation therapy [2]

Note: Lack of evidence of any benefit. Use of this therapy may cause renal tubular necrosis, arrhythmia, hypocalcemia, marrow depression, bleeding, hypotension or allergic reactions.

Recommendation

- Chelation therapy is **NOT** recommended in IHD patients.

Grade of Recommendation: B (Moderate recommendation)

Fish oils

Recommendation

- ❖ No recommendation available.

Ethanol

Note: light ethanol use raises HDL-C types II and II. It also increases fibrinolysis, and decreases platelet aggregation and insulin resistance.

Recommendation

- ❖ The cardiovascular benefits of ethanol must be weighed against potential associated negative effects, e.g. breast cancer, weight gain, elevated triglycerides, gastrointestinal disturbance, hypertension and accidents due to impairment.

  Grade of Recommendation: C (Weak recommendation)

Stress management and behavior modification

Note: Individual and group stress management reduce psychological distress, blood pressure, heart rate, cardiac morbidity and mortality in meta-analyses of randomized controlled trials.

Recommendation

- ❖ Due to difficulties in generalizing from the evidence, no specific recommendation is made.

M121

IMPORTANT NOTE CONCERNING THE FOLLOWING PAGES

THE PAGES WHICH FOLLOW HAVE BEEN FILMED TWICE IN ORDER TO OBTAIN THE BEST REPRODUCTIVE QUALITY

USERS SHOULD CONSULT ALL THE PAGES REPRODUCED ON THE FICHE IN ORDER TO OBTAIN A COMPLETE READING OF THE TEXT.

REMARQUE IMPORTANTE CONCERNANT LES PAGES QUI SUIVENT

LES PAGES SUIVANTES ONT ÉTÉ REPRODUITES EN DOUBLE AFIN D'AMÉLIORER LA QUALITÉ DE REPRODUCTION

LES UTILISATEURS DOIVENT CONSULTER TOUTES LES PAGES REPRODUITES SUR LA FICHE AFIN D'OBTENIR LA LECTURE DU TEXTE INTÉGRAL

micromedia
a division of IHS Canada

20 Victoria Street
Toronto, Ontario M5C 2N8
Tel.: (416) 362-5211
Toll Free: 1-800-387-2689
Fax: (416) 362-6161
Email: info@micromedia.on.ca

Appendix C

Body Mass Index (kg/m^2)

Height (m)	Weight (Kg) 45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130
1.50	20.0	22.2	24.4	26.7	28.9	31.1	33.3	35.6	37.8	40.0	42.2	44.4	46.7	48.9	51.1	53.3	55.6	57.8
1.55	18.7	20.8	22.9	25.0	27.1	29.1	31.2	33.3	35.4	37.5	39.5	41.6	43.7	45.8	47.9	49.9	52.0	54.1
1.60	17.6	19.5	21.5	23.4	25.4	27.3	29.3	31.3	33.2	35.2	37.1	39.1	41.0	43.0	44.9	46.9	48.8	50.8
1.65	16.5	18.4	20.2	22.0	23.9	25.7	27.5	29.4	31.2	33.1	34.9	36.7	38.6	40.4	42.2	44.1	45.9	47.8
1.70	15.6	17.3	19.0	20.8	22.5	24.2	26.0	27.7	29.4	31.1	32.9	34.6	36.3	38.1	39.8	41.5	43.3	45.0
1.75	14.7	16.3	18.0	19.6	21.2	22.9	24.5	26.1	27.8	29.4	31.0	32.7	34.3	35.9	37.6	39.2	40.8	42.4
1.80	13.9	15.4	17.0	18.5	20.1	21.6	23.1	24.7	26.2	27.8	29.3	30.9	32.4	34.0	35.5	37.0	38.6	40.1
1.85	13.1	14.6	16.1	17.5	19.0	20.5	21.9	23.4	24.8	26.3	27.8	29.2	30.7	32.1	33.6	35.1	36.5	38.0
1.90	12.5	13.9	15.2	16.6	18.0	19.4	20.8	22.2	23.5	24.9	26.3	27.7	29.1	30.5	31.9	33.2	34.6	36.0
1.95	11.8	13.1	14.5	15.8	17.1	18.4	19.7	21.0	22.4	23.7	25.0	26.3	27.6	28.9	30.2	31.6	32.9	34.2
2.00	11.3	12.5	13.8	15.0	16.3	17.5	18.8	20.0	21.3	22.5	23.8	25.0	26.3	27.5	28.8	30.0	31.3	32.5
2.05	10.7	11.9	13.1	14.3	15.5	16.7	17.8	19.0	20.2	21.4	22.6	23.8	25.0	26.2	27.4	28.6	29.7	30.9
2.10	10.2	11.3	12.5	13.6	14.7	15.9	17.0	18.1	19.3	20.4	21.5	22.7	23.8	24.9	26.1	27.2	28.3	29.5
2.15	9.7	10.8	11.9	13.0	14.1	15.1	16.2	17.3	18.4	19.5	20.6	21.6	22.7	23.8	24.9	26.0	27.0	28.1
2.20	9.3	10.3	11.4	12.4	13.4	14.5	15.5	16.5	17.6	18.6	19.6	20.7	21.7	22.7	23.8	24.8	25.8	26.9
2.25	8.9	9.9	10.9	11.9	12.8	13.8	14.8	15.8	16.8	17.8	18.8	19.8	20.7	21.7	22.7	23.7	24.7	25.7
2.30	8.5	9.5	10.4	11.3	12.3	13.2	14.2	15.1	16.1	17.0	18.0	18.9	19.8	20.8	21.7	22.7	23.6	24.6

NOTE: Ideal body mass index: 20-25 (shaded area)

Appendix C

Body Mass Index (kg/m^2)

Height (m)	Weight (Kg) 45	50	55	60	65	70	75	80	85	90	95	100	105	110	115	120	125	130
1.50	20.0	22.2	24.4	26.7	28.9	31.1	33.3	35.6	37.8	40.0	42.2	44.4	46.7	48.9	51.1	53.3	55.6	57.8
1.55	18.7	20.8	22.9	25.0	27.1	29.1	31.2	33.3	35.4	37.5	39.5	41.6	43.7	45.8	47.9	49.9	52.0	54.1
1.60	17.6	19.5	21.5	23.4	25.4	27.3	29.3	31.3	33.2	35.2	37.1	39.1	41.0	43.0	44.9	46.9	48.8	50.8
1.65	16.5	18.4	20.2	22.0	23.9	25.7	27.5	29.4	31.2	33.1	34.9	36.7	38.6	40.4	42.2	44.1	45.9	47.8
1.70	15.6	17.3	19.0	20.8	22.5	24.2	26.0	27.7	29.4	31.1	32.9	34.6	36.3	38.1	39.8	41.5	43.3	45.0
1.75	14.7	16.3	18.0	19.6	21.2	22.9	24.5	26.1	27.8	29.4	31.0	32.7	34.3	35.9	37.6	39.2	40.8	42.4
1.80	13.9	15.4	17.0	18.5	20.1	21.6	23.1	24.7	26.2	27.8	29.3	30.9	32.4	34.0	35.5	37.0	38.6	40.1
1.85	13.1	14.6	16.1	17.5	19.0	20.5	21.9	23.4	24.8	26.3	27.8	29.2	30.7	32.1	33.6	35.1	36.5	38.0
1.90	12.5	13.9	15.2	16.6	18.0	19.4	20.8	22.2	23.5	24.9	26.3	27.7	29.1	30.5	31.9	33.2	34.6	36.0
1.95	11.8	13.1	14.5	15.8	17.1	18.4	19.7	21.0	22.4	23.7	25.0	26.3	27.6	28.9	30.2	31.6	32.9	34.2
2.00	11.3	12.5	13.8	15.0	16.3	17.5	18.8	20.0	21.3	22.5	23.8	25.0	26.3	27.5	28.8	30.0	31.3	32.5
2.05	10.7	11.9	13.1	14.3	15.5	16.7	17.8	19.0	20.2	21.4	22.6	23.8	25.0	26.2	27.4	28.6	29.7	30.9
2.10	10.2	11.3	12.5	13.6	14.7	15.9	17.0	18.1	19.3	20.4	21.5	22.7	23.8	24.9	26.1	27.2	28.3	29.5
2.15	9.7	10.8	11.9	13.0	14.1	15.1	16.2	17.3	18.4	19.5	20.6	21.6	22.7	23.8	24.9	26.0	27.0	28.1
2.20	9.3	10.3	11.4	12.4	13.4	14.5	15.5	16.5	17.6	18.6	19.6	20.7	21.7	22.7	23.8	24.8	25.8	26.9
2.25	8.9	9.9	10.9	11.9	12.8	13.8	14.8	15.8	16.8	17.8	18.8	19.8	20.7	21.7	22.7	23.7	24.7	25.7
2.30	8.5	9.5	10.4	11.3	12.3	13.2	14.2	15.1	16.1	17.0	18.0	18.9	19.8	20.8	21.7	22.7	23.6	24.6

NOTE: Ideal body mass index: 20-25 (shaded area)